Remarks

I. Claim Amendments

In an effort to expedite prosecution of the pending claims to allowance, and in Applicant's view because it will have no substantive effect on the proper scope of the pending claims, Applicants have amended Claim 1 to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention. No new matter has been added.

II. Claim Rejections – 35 U.S.C. §112

Applicants respectfully disagree with the Action's assertion that claim 1 does not require the expression of a recombinant antibody in the claimed host cell Nevertheless, in an effort to expedite prosecution of the pending claims to allowance, and in Applicant's view because it will have no substantive effect on the proper scope of the pending claims, Applicant has amended claim 1 to recite a recombinant *E. coli* host cell comprising a gene encoding a recombinant antibody, and a gene encoding an endogenous protein that has at least one genetic alteration that results in modification of at least one physical property of the endogenous protein such that the endogenous protein does not co-purify with the recombinant antibody. Applicant, therefore, respectfully requests withdrawal of the objection and rejection in view of the amendments.

III. §102(b) Anticipation

A. Shuman

Claims 1-4 and 11 have been rejected under 35 U.S.C §102(b) as anticipated by Shuman *et al.* The Office Action asserts that Shuman discloses an *E. coli* strain comprising a deletion of the gene encoding the maltose binding protein, which would affect the isoelectric point of the resulting protein. The Office Action further asserts that the claims do not require that a recombinant antibody is expressed in the claimed host cell.

Applicants respectfully disagree with the Office's interpretation that Claim 1 does not require that a recombinant antibody is expressed in the claimed host cell. However, in order to expedite prosecution of the application, Applicants have amended Claim 1 to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention. In

addition, Applicant contends that the amendments to claim 1 have no substantive effect on the proper scope of the pending claims.

With respect to the rejection based upon Shuman *et al.*, Applicant notes that while Shuman *et al.* disclose an *E. coli* strain comprising a deletion of the gene encoding maltose binding protein, this reference does not disclose an *E. coli* strain that either expresses an antibody or that comprises a gene with an alteration that affects the isoelectric point such that the product of the modified gene no longer co-purifies with the recombinant antibody expressed by the cell. Applicants believe that in light of the amendments made herein, this rejection is improper, and request that it be withdrawn.

B. Joly

Claims 1-5, 11, and 12 have been rejected under 35 U.S.C. §102(b) as being anticipated by Joly *et al.* The Office Action asserts that Joly *et al.* disclose an *E. coli* strain comprising at least one genetic alteration that results in the modification of at least one physical property of at least one endogenous protein (*i.e.*, PstS) that co-purifies with a recombinant antibody expressed by the cell.

Applicant respectfully disagrees with the Action's characterization of Joly *et al.* Applicant notes that Joly *et al.* disclose an *E. coli* strain expressing a heterologous protein and further comprising a *pstS (phoS)* gene with an altered phosphate-binding region. However, this reference does not disclose that the altered *pstS* gene results in a change in the PstS protein such that the PstS protein would no longer co-purify with the heterologous protein expressed in the cell. This reference also does not teach that the heterologous protein being expressed is a recombinant antibody. Furthermore, a change in the Psts (PhoS) phosphate-binding site does not necessarily result in a change of the isolectric point of the protein. Joly *et al.* fail to disclose a change to the overall hydrophobicity or charge of the protein. A person skilled in the art would recognize that the crystal structure of PstS/PhoS shows that the phosphate binding site of PstS is buried 8Å below the protein surface (Leucke and Quiocho, 1990, *Nature* 347: 402-406, *see* p. 403, right hand column, second paragraph). As Joly *et al.* disclose changing amino acid residues present in this binding site, this reference does not disclose altering the isoelectric point of the PstS protein by altering amino acids located on the surface of the PstS protein. Applicants

believe that in light of the amendments made herein, this rejection is improper, and request that it be withdrawn.

C. Bass

Claims 1-5, 11 and 12 have been rejected under 35 U.S.C. §102(b) as being anticipated by Bass *et al.* The Office Action asserts that Bass *et al.*disclose an *E. coli* strain comprising at least one genetic alteration that results in the modification of at least one physical property of at least one endogenous protein that co-purifies with a recombinant antibody expressed by the cell which is PstS.

Applicant respectfully disagrees with the Action's characterization of Bass *et al.* Applicant notes that Bass *et al.* disclose an *E. coli* strain encoding a PstS variant having an amino acid variation within the phosphate-binding region of the corresponding native PstS, and expressing a polypeptide of interest. However, the Bass *et al.* reference, like Joly *et al.*, does not disclose that the altered *pstS* gene results in a change in the PstS protein that results in the PstS protein not co-purifying with the heterologous protein expressed in the cell. As Bass *et al.* disclose changing amino acid residues present in this binding site, this reference does not disclose altering the isoelectric point of the PstsS protein by altering amino acids located on the surface of the PstS protein. Applicants believe that in light of the amendments made herein, this rejection is improper, and request that it be withdrawn.

D. Opper

Claims 1-5, 11 and 12 have been rejected under 35 U.S.C. §102(b) as being anticipated by Opper *et al.* The Office Action assert that Opper *et al.* disclose an *E. coli* strain comprising at least one genetic alteration that results in a modification of at least one physical property of at least one endogenous protein (*i..e.*, thioredoxin) that co-purifies with a recombinant antibody expressed by the cell.

Applicant disagrees with the Action's characterization of Opper *et al.* Applicant notes that the Abstract of the Opper *et al.* reference appears to disclose the production of recombinant antibodies (or Ab fragments, or Ab fragment/enzyme fusion proteins, wherein the enzyme is a cytoplasmic mammalian or *E. coli* enzyme) where the antibody is produced in a thioredoxinreductase deficient *E .coli* strain. This reference does not disclose that the genetic alteration, presumably in the thioredoxin reductase gene, changes the property of that protein

such that it does not co-purify with a recombinant antibody, where the wildtype protein would co-purify with the recombinant antibody. Applicants believe that in light of the amendments made herein, this rejection is improper, and request that it be withdrawn.

Applicant respectfully contends that the cited references do not anticipate the claimed invention, and respectfully request the withdrawal of the anticipation rejections.

IV. Conclusion

Applicant submits that the application is now in condition for allowance. Applicant invites the Examiner to contact the Applicant's undersigned representative at (312) 913-3319 if the Examiner believes that this would expedite prosecution of this application.

Respectfully submitted,

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